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Clinical presentation, management and outcomes in the Acute Heart Failure Global Survey of Standard Treatment (ALARM-HF)

Follath, F ; Yilmaz, M B ; Delgado, J F ; Parissis, J T ; Porcher, R ; Gayat, E ; Burrows, N ; McLean, A ; Vilas-Boas, F ; Mebazaa, A

Abstract: **PURPOSE:** We performed a survey on acute heart failure (AHF) in nine countries in four continents. We aimed to describe characteristics and management of AHF among various countries, to compare patients with de novo AHF versus patients with a pre-existing episode of AHF, and to describe subpopulations hospitalized in intensive care unit (ICU) versus cardiac care unit (CCU) versus ward. **METHODS AND RESULTS:** Data from 4,953 patients with AHF were collected via questionnaire from 666 hospitals. Clinical presentation included decompensated congestive HF (38.6%), pulmonary oedema (36.7%) and cardiogenic shock (11.7%). Patients with de novo episode of AHF (36.2%) were younger, had less comorbidities and lower blood pressure despite greater left ventricular ejection fraction (LVEF) and were more often admitted to ICU. Overall, intravenous (IV) diuretics were given in 89.7%, vasodilators in 41.1%, and inotropic agents (dobutamine, dopamine, adrenaline, noradrenaline and levosimendan) in 39% of cases. Overall hospital death rate was 12%, the majority due to cardiogenic shock (43%). More patients with de novo AHF (14.2%) than patients with a pre-existing episode of AHF (10.8%) ($p = 0.0007$) died. There was graded mortality in ICU, CCU and ward patients with mortality in ICU patients being the highest (17.8%) ($p < 0.0001$). **CONCLUSIONS:** Our data demonstrated the existence of different subgroups based on de novo or pre-existing episode(s) of AHF and the site of hospitalization. Recognition of these subgroups might improve management and outcome by defining specific therapeutic requirements.

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(38.6%), pulmonary oedema (36.7%) and cardiogenic shock (11.7%). Patients with de novo episode of AHF (36.2%) were younger, had less comorbidities and lower blood pressure despite greater left ventricular ejection fraction (LVEF) and were more often admitted to ICU. Overall, intravenous (IV) diuretics were given in 89.7%, vasodilators in 41.1%, and inotropic agents (dobutamine, dopamine, adrenaline, noradrenaline and levosimendan) in 39% of cases. Overall hospital death rate was 12%, the majority due to cardiogenic shock (43%). More patients with de novo AHF (14.2%) than patients with a pre-existing episode of AHF (10.8%) ($p = 0.0007$) died. There was graded mortality in ICU, CCU and ward patients with mortality in ICU patients being the highest (17.8%) ($p < 0.0001$). *Conclusions:* Our data demonstrated the existence of different subgroups based on de novo or pre-existing episode(s) of AHF and the site of hospitalization. Recognition of these subgroups might improve management and outcome by defining specific therapeutic requirements.

Keywords Acute heart failure syndromes · Classification · Management · Prognosis · Therapy

Introduction

Acute heart failure (AHF) is one of the most frequent reasons for hospitalization in western countries. Despite its clinical importance, AHF receives much less attention than chronic heart failure (CHF) and has normally not been the subject of large scale studies [1]. More recently, the development of new therapeutic agents, such as nesiritide and levosimendan, has stimulated the interest in AHF syndromes. Several epidemiological surveys in Europe [2–5] (Zürich-Helsinki; Euro Heart Survey II, EHS II; Italian Acute Heart Failure Survey; *Etude Française de l'Insuffisance Cardiaque Aigue* the French Study of Acute Heart Failure, EFICA) and the USA [6] (Acute Decompensated Heart Failure National Registry, ADHERE) provided several clues for diagnosis and classification of these syndromes. A task force of the European Society of Cardiology (ESC) and the European Society of Intensive Care Medicine (ESICM) has developed guidelines for the diagnosis and treatment of AHF, including a clinical classification based on clinical presentation [7]. In one-third of patients AHF was the first episode of cardiac decompensation in EHFS II. These de novo episodes of AHF have also been described to have a worse outcome than the following episodes of AHF in Europe [3]. The prevalence and the outcome of de novo episodes of AHF compared with the other episodes need to be further explored in a more global database. On the other hand, with the exception of EFICA, in which intensive care unit (ICU) and cardiac care unit (CCU) patients were combined with scant details, no differentiation has been done so far on AHF patients hospitalized in ICU versus CCU and wards.

The objectives of the international Acute Heart Failure Global Registry of Standard Treatment (ALARM-HF) were to describe characteristics and management of hospitalized AHF patients among various countries, to compare patients with de novo AHF versus patients with pre-existing episode(s) of AHF, and to describe subpopulations hospitalized in ICU versus CCU versus ward.

Methods

Survey description

The ALARM-HF global survey collected anonymised data from 4,953 patients in nine countries: France, Germany, Italy, Spain, UK, Greece, Turkey, Australia and Mexico. AHF was the final diagnosis for all studied patients based on ESC/ESICM guidelines [7]. The study was conducted as a retrospective in-hospital chart audit survey, via questionnaire, from 666 hospitals. The hospital sample was recruited to be representative according to geographic region, hospital size (number of beds),

sector (public vs. private) and type (university vs. non-teaching status). The study was carried out according to the principles of the Declaration of Helsinki and approved by all local ethics committees.

Patient inclusion

The paper-based data collection was conducted over the period from October 2006 to March 2007. Patient care report forms (CRFs), which included 20 discrete questions with subdivisions, were completed by the attending physician after 5–8 consecutive AHF cases were discharged, based on medical records. Patients were classified by responsible cardiologists or ICU physicians according to ESC/ESICM guidelines (2005) as those with de novo (first time) AHF and those with pre-existing episode(s) of AHF. There was no exclusion criterion.

Patient evaluation

Clinical history, signs and symptoms, and medication (admission as well as discharge) were recorded. The pre-hospital medical history including previous heart failure, coronary artery disease, hypertension, diabetes, atrial fibrillation, chronic renal disease and precipitating factors such as acute coronary syndromes, arrhythmias, and valve dysfunction were entered into the CRF. Details of intravenous drugs administered for AHF, including timing and site of initiation, as well as dosage and duration were also registered. Where available, echocardiography data were collected at diagnosis and/or prior to discharge. Except for B-type natriuretic peptide (BNP) (93.8% missing data) and left ventricular ejection fraction (LVEF) (33.7% missing data), missing data were very infrequent. Thus, 78.3% of the patients had complete datasets, and 96.4% had at least 90% complete data. Patients were subclassified into three categories: those who were referred to intensive care unit (ICU) or cardiac care unit (CCU) for at least 24 h during hospital stay or those who were referred only to wards and never visited ICU or CCU during hospital stay (ward).

Statistics

The statistical analyses were conducted by the Département de Biostatistique et Informatique Médicale, Hôpital Saint Louis, Paris, France.

Categorical variables are presented as counts and percentages, and quantitative variables as medians and interquartile range (IQR). LVEF was an exception for which mean and standard deviation (SD) are given. Subgroups of patients were compared by using chi-square tests for categorical variables and Wilcoxon rank-sum tests for

quantitative variables. Age categories were compared by using the chi-square test for trends. Changes of prescription rates between admission and discharge were assessed by using McNemar's test. The cumulative incidence of hospital death during follow-up was estimated in a competing risks framework, with discharge alive as the competing event. Length of stay (LOS) for patients transferred to another hospital or to another ward of the same hospital was recorded at the time of transfer. Cumulative incidence curves were compared by using Gray's test. All tests were two-sided, and p values less than 0.05 were considered as indicating significant differences. Analyses were carried out using R 2.5.1 statistical software (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Epidemiology classification

The ALARM-HF survey included a total of 4,953 patients, with a median age between 66 and 70 years for the whole cohort, from nine countries (France 588, Germany 617, Italy 679, Spain 700, UK 623, Greece 255, Turkey 628, Mexico 601 and Australia 262), admitted to 666 hospitals of different size and type, managed by cardiologists or intensive care physicians. The presenting symptoms and clinical findings were dyspnoea at rest (73%), pulmonary rales (61%), orthopnoea (56%), fatigue (44%), peripheral oedema (43%), raised jugular venous pressure (40%), cold extremities (26%) and weight gain (25%) in the whole cohort.

Of the 4,953 patients, the distribution by countries is presented in Fig. 1; as a whole, 36.2% had de novo

AHF, and 63.8% had a pre-existing episode of AHF. Clinical presentation was decompensated congestive HF (38.6%), pulmonary oedema (36.7%), cardiogenic shock (11.7%), hypertensive HF (7.4%), right HF (4.5%) and high-output HF (1.1%). The demographic characteristics, comorbidities and precipitating factors are presented in Table 1.

Patients with de novo AHF were younger and had less comorbidities than those with a pre-existing episode of AHF. Acute coronary syndromes were the main cause of AHF in patients with de novo AHF, whereas arrhythmias, infections and non-compliance to chronic medications were the most frequent precipitating factors in patients with pre-existing episode(s) of AHF. The mean LVEF was $40 \pm 15\%$ in patients with de novo AHF versus $37 \pm 14\%$ in patients with a pre-existing episode of AHF ($p < 0.0001$). Systolic (SBP) and diastolic blood pressure (DBP) at admission were lower, and pulmonary oedema and cardiogenic shock were more frequent in patients with de novo AHF (Table 2). Furthermore, patients presenting with de novo AHF were more frequently referred to ICU than to CCU and ward (68% vs. 42.8% vs. 48.2%, respectively, $p < 0.0001$) on admission.

Overall, 2,247 patients had been in ICU versus 1,475 patients in CCU versus 1,231 patients who had not been either in ICU or in CCU (only wards).

ICU and CCU patients were relatively younger compared with ward patients. Both hypertension and diabetes mellitus were more frequent in ICU patients. On the other hand, mean LVEF was $39 \pm 15\%$ in ICU patients versus $36 \pm 13\%$ in CCU patients versus $40 \pm 15\%$ in ward patients ($p < 0.0001$). Systolic (SBP) and diastolic blood pressure (DBP) at admission were lowest, BNP levels were the highest, and oliguria-anuria and cardiogenic shock were most frequent in the ICU patients (Table 2).

Fig. 1 Stacked bar graph showing distribution of six discrete diagnoses of ESC classification among participating countries, compared with Euro Heart Survey (EHS HF II)

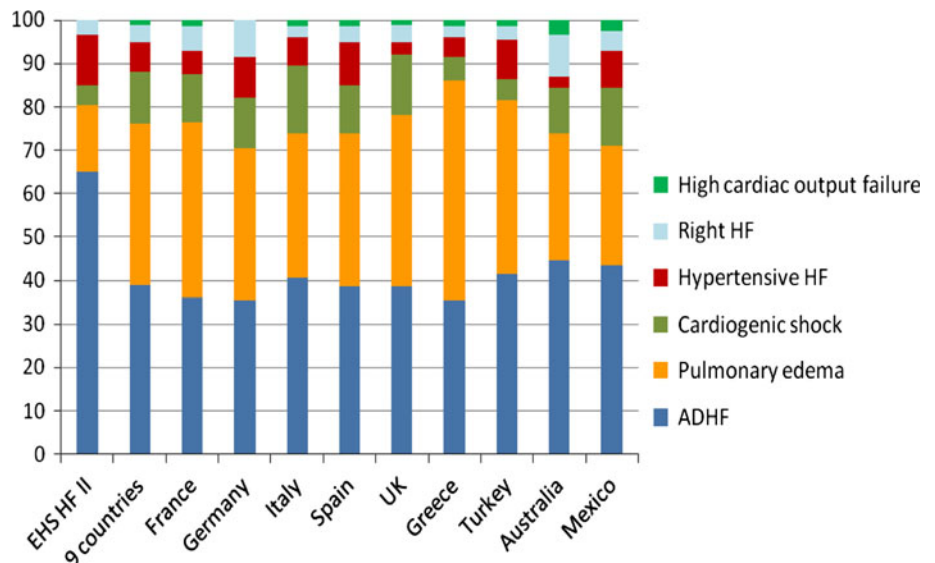


Table 1 Underlying diseases and precipitating factors of ALARM-HF patients

Characteristics	Total	De novo AHF		<i>p</i> value de novo AHF, yes versus no	Patients hospitalized in			<i>p</i> values among ICU, CCU, ward patients
		Yes	No ^b		ICU	CCU	Ward	
Patients, <i>n</i> (%)	4,953	1,792 (36.2)	3,161 (63.8)		2,247 (45.4)	1,475 (29.8)	1,231 (24.8)	
Age (years)				<0.0001				<0.0001
<50	9.5	15.4	6.2		10.3	9.6	8.2	
51–60	16.5	18.0	15.7		18.0	18.8	11.1	
61–70	29.3	28.4	29.8		30.6	29.8	26.2	
71–80	29.8	26.1	31.8		28.4	27.9	34.4	
>80	14.9	12.1	16.5		12.7	13.9	20.1	
Male gender (%)	62.4	63.6	61.7	0.19	62.4	66.9	57.0	<0.0001
Underlying diseases								
Chronic systolic heart failure (%)	36.4	2.6	55.4	<0.0001	35.8	32.1	42.5	<0.0001
Coronary artery disease (%)	30.7	25.4	33.7	<0.0001	29.4	34.2	28.8	0.002
Hypertension (%) ^a	70.2	66.3	72.4	<0.0001	73.2	68.1	67.3	0.00014
Diabetes (%)	45.3	38.8	49.0	<0.0001	47.9	44.1	42.2	0.003
Atrial fibrillation/flutter (%)	24.4	13.4	30.6	<0.0001	22.2	22.6	30.5	<0.0001
Chronic renal disease (as reported) (%)	21.4	11.0	27.1	<0.0001	21.2	20.8	22.4	0.60
Anaemia (%)	14.4	8.9	17.4	<0.0001	15.7	12.4	14.2	0.024
COPD/asthma (%)	24.8	15.8	29.7	<0.0001	25.9	23.3	24.4	0.21
Pacemaker (%)	5.5	2.2	7.4	<0.0001	3.9	6.4	7.6	<0.0001
Cardiomyopathy (%)	12.6	6.2	16.3	<0.0001	11.3	13.0	14.6	0.019
Precipitating factors (on admission)								
Acute coronary syndrome (%)	36.9	48.6	30.2	<0.0001	40.9	45.9	18.8	<0.0001
Arrhythmia (%)	26.9	19.1	31.3	<0.0001	27.9	24.9	27.3	0.13
Infection (%)	16.3	12.1	18.7	<0.0001	18.9	12.1	16.7	<0.0001
Poor compliance with medications (%)	13.4	2.2	19.7	<0.0001	10.9	12.2	19.4	<0.0001

ICU intensive care unit, CCU cardiac care unit, AHF acute heart failure, COPD chronic obstructive pulmonary disease, ICU/CCU at least 1 day hospital stay in ICU or CCU, ward no stay in ICU or CCU

Exact age was not recorded, but only 5-year age categories. Median age was between 66 and 70 years for the whole cohort, and for

patients admitted to ICU and CCU. Patients admitted to the ward had median age between 71 and 75 years old

^a Systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or receiving treatment with antihypertensive medication

^b Pre-existing episode(s) of AHF

Management

The site of initial management and intravenous drug administration was the emergency room in 74%. The remaining patients received initial treatment in the ICU in 10%, CCU in 7%, a cardiology ward in 5% and a general medicine ward in 2%.

Details of drug treatment and other therapeutic measures are presented in Table 3. Overall, IV diuretics were given in 89.7%, vasodilators (mainly nitroglycerine) in 41.1%, inotropic agents in 39% (dobutamine 22.3%, dopamine 13%, adrenaline and noradrenaline 7.8%, and levosimendan in 6.4%) of cases. Distribution of drug utilization among the nine studied countries is detailed in Fig. 2.

Table 3 further shows that IV nitrate was more frequently used among patients in CCU, whereas, all classes of inotropes were most frequently utilized in patients referred to ICU.

Other important initial non-pharmacological measures were respiratory support by CPAP in 9.6%, mechanical ventilation in 16.2%, percutaneous coronary intervention (PCI) 12.8%, and cardioversion 7.8% in the whole cohort. CPAP, mechanical ventilation and cardioversion rates were most frequent in ICU patients (Table 3).

Outcomes

Overall hospital death rate was 12%, the majority due to cardiogenic shock (43%). More patients with de novo AHF (14.2%) than patients with a pre-existing episode of AHF (10.8%) ($p = 0.0007$) died (Table 4).

There was graded mortality in ICU, CCU and ward patients (Table 4 and Fig. 3). Hospital mortality in ICU

Table 2 Hemodynamics and initial findings by de novo or pre-existing episode(s) of AHF and by ICU versus CCU versus ward

Variable	De novo AHF		<i>p</i> value	Patients hospitalized in			<i>p</i> value ^b
	Yes, <i>n</i> = 1,792	No, <i>n</i> = 3,161		ICU, <i>n</i> = 2,247	CCU, <i>n</i> = 1,475	Ward, <i>n</i> = 1,231	
Median SBP (mmHg) (IQR)	130 (95–160)	130 (103–160)	<0.0001	120 (95–160)	130 (100–160)	140 (110–160)	<0.0001
SBP < 100 (mmHg), no. (%)	466 (26.3)	549 (17.5)	<0.0001	617 (27.7)	298 (20.3)	100 (8.3)	<0.0001
Median DBP (mmHg) (IQR)	75 (60–90)	80 (60–95)	<0.0001	78 (58–95)	80 (60–94)	80 (70–95)	<0.0001
Heart rate, median (IQR)	110 (90–122)	107 (90–120)	0.002	110 (90–125)	110 (90–120)	100 (86–118)	<0.0001
Cardiogenic shock (%)	19.1	7.5	<0.0001	16.2	12.3	2.9	<0.0001
Pulmonary edema (%)	39.8	35.0	0.0008	38.1	42.8	27.0	<0.0001
Cold extremities (%)	29.3	24.3	0.0001	33.1	26.2	13.2	<0.0001
Normal diuresis at baseline (%)	55.2	52.6	0.093	47.2	54.3	65.5	<0.0001
Median BNP (IQR) ^a	908 (415–1,572)	1,040 (576–2,212)	0.020	1108 (552–1,995)	1045 (642–2,136)	700 (313–1,640)	0.009

SBP systolic blood pressure, DBP diastolic blood pressure

^a BNP recorded in 307 patients

^b *p* among ICU versus CCU versus ward

Table 3 Treatment during hospitalization ICU versus CCU versus ward

Treatment performed	Patients hospitalized in				<i>p</i> value
	All, <i>n</i> = 4,953 (%)	ICU, <i>n</i> = 2,247 (%)	CCU, <i>n</i> = 1,475 (%)	Ward, <i>n</i> = 1,231 (%)	
CPAP	9.6	15.8	6.3	2.2	<0.0001
Mechanical ventilation	16.2	30.0	6.8	2.3	<0.0001
Oral diuretic	60.5	49.1	65.7	75.0	<0.0001
IV diuretic	89.7	89.9	90.3	88.5	0.30
Oral spironolactone/eplerenone	27.5	23.4	28.6	33.7	<0.0001
IV nitrate	41.1	44.0	48.5	27.2	<0.0001
Beta-blocker	37.8	30.7	45.2	42.1	<0.0001
IV inotrope					
Adrenaline	3.6	6.6	1.5	0.7	<0.0001
Dobutamine	22.3	30.3	21.8	8.2	<0.0001
Dopamine	13.0	16.0	14.2	6.1	<0.0001
Levosimendan	6.4	7.7	7.3	3.1	<0.0001
Noradrenaline	4.2	8.2	1.3	0.2	<0.0001
Amiodarone	2.6	3.2	2.6	1.7	0.037
Heparin (UFH)	2.0	3.1	1.7	0.2	<0.0001
LMWH	1.0	1.5	0.5	0.8	0.0089
PCI	12.8	13.4	19.1	4.1	<0.0001
CABG	3.0	4.5	2.6	0.7	<0.0001
IABP	4.8	6.1	6.6	0.4	<0.0001
Pacemaker	2.5	3.2	2.4	1.1	0.00085
ICD	1.7	1.2	2.5	1.6	0.0071
Valvular surgery	3.5	5.2	2.5	1.5	<0.0001
Cardioversion	7.8	9.5	6.4	6.3	0.0003

CPAP continuous positive airway pressure, UFH unfractionated heparin, LMWH low molecular weight heparin, PCI percutaneous coronary intervention, CABG coronary artery bypass grafting, ICD

implantable cardioverter defibrillator, IABP intraaortic balloon counterpulsation

patients was highest (17.8%), $p < 0.0001$. A need for referral to ICU seemed to impact negatively not only the mortality but also the length of stay in the hospital (Table 4).

Discussion

ALARM-HF is a large survey of hospitalized AHF patients, including the identification of a large subgroup

Fig. 2 Bar graph showing treatment strategies, namely intravenous diuretics, intravenous vasodilators and inotropes, among participating countries

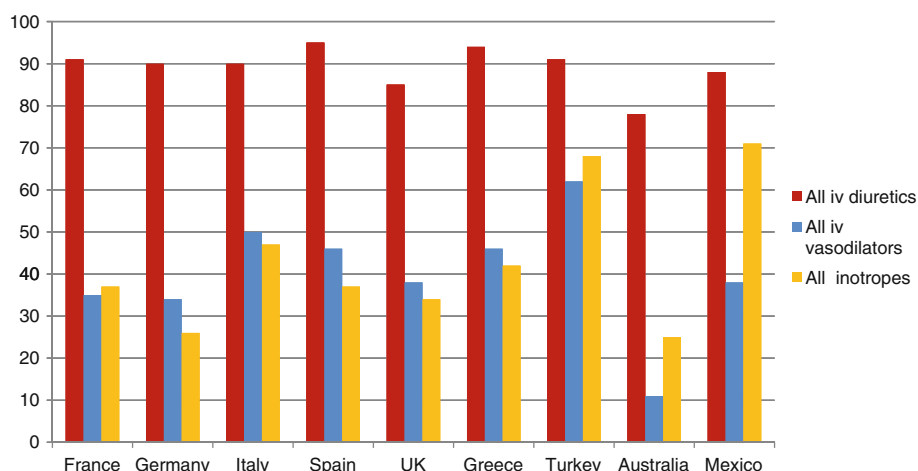


Table 4 Outcomes and length of stay in ALARM-HF study

	Total, <i>n</i> = 4,953	De novo AHF		Patients hospitalized in			<i>p</i> value ^a
		Yes, <i>n</i> = 1,792	No, <i>n</i> = 3,161	ICU, <i>n</i> = 2,247	CCU, <i>n</i> = 1,475	Ward, <i>n</i> = 1,231	
Outcome no.							
Transfer	752	360	392	486	203	63	
Death	529	221	308	334	141	54	
Discharge	3,672	1,211	2,461	1,427	1,131	1,114	
LOS (days), median (IQR)	6 (4–10)	6 (4–10)	7 (4–10)	7 (4–11)	6 (4–9)	6 (4–9)	<0.0001
Hospital mortality at 24 h, (%)	3.5	4.2	3.1	4.0	3.9	2.1	0.80
Overall hospital mortality, (%)	12.0	14.2	10.8	17.8	10.5	4.5	<0.0001
ICU/CCU stay (days), median (IQR)	3 (2–6)	3 (2–6)	3 (2–6)	4 (2–6)	3 (2–5)	–	

LOS is reported for all patients (including in-hospital deaths and transfers). LOS in ICU/CCU for patients admitted to these units

^a *p* for ICU versus CCU versus ward

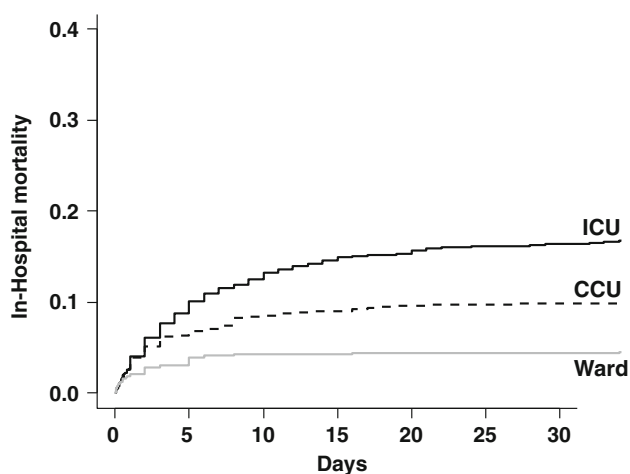


Fig. 3 In-hospital mortality in patients hospitalized in ICU or CCU for at least 24 h and in the ward without stay in either ICU or CCU (ward)

of de novo AHF patients, and a detailed documentation of the site and mode of treatment in ICU, CCU and wards, respectively. ALARM-HF showed that the first episode of

AHF was more severe with a worse outcome than the following episodes of AHF. In addition, there was a graded severity in patients hospitalized in ICU versus CCU and ward.

The total in-hospital mortality of ALARM (12%) was higher than the Italian survey (7.3%), EHFS II (6.7%) and ADHERE (4%) and lower than EFICA (27%) [3–5, 6]. Those differences are driven by many factors including the incidence of 11.7% of cardiogenic shock in the present cohort and the severity of ALARM patients as seen by high prevalence of patients hospitalized in ICU and CCU.

In most surveys and trials dealing with AHF, no distinction was made between the first episode (de novo) and the following episodes of AHF [2, 4, 10]. ALARM-HF confirms that an AHF episode was more deadly when it occurred for the first time (14 vs. 10% in de novo AHF and AHF with pre-existing episodes). Our study further describes important clinical differences between the two groups of patients including a lower systolic blood pressure at admission and a higher incidence of acute coronary syndrome as a precipitating factor (48.6 vs.

30.2% in de novo AHF and in AHF with pre-existing episodes) that both could possibly influence for worse outcomes among patients with de novo AHF [8]. Some other hypotheses can also be raised regarding the greater severity of the first AHF episode. This includes the activation of different pathways, such as the extent of sympathetic nervous system activation, that may be different in patients with de novo AHF and in patients with a pre-existing episode of AHF. Paradoxically, a lower mortality of AHF was observed in patients with pre-existing CHF despite a more frequent history of atrial fibrillation and of arrhythmia as precipitating factors, as well as more frequent renal disease and more frequent comorbidities, including COPD. On the other hand, patients with a pre-existing episode of AHF received medications before admission that might have altered the severity of the AHF episode. Accordingly, ALARM-HF emphasizes the need to stratify AHF in future surveys and trials as de novo AHF and AHF with pre-existing episodes. Indeed, a new treatment might be more effective in one of the two categories of AHF episode.

Presentation of figures comparing ICU versus CCU versus ward is one of the unique features of the present manuscript. With the exception of ADHERE [6], which combined ICU/CCU, graded severity and mortality was presented for the first time. In the present study, ALARM shows that patients admitted to the ICU had more hypertension and diabetes as underlying diseases and presented with more cardiogenic shock, lower systolic and diastolic blood pressure, more frequent oliguria-anuria and peripheral hypoperfusion than the other AHF patients. Although not recorded, severity scores are very likely worse in patients admitted to ICU. Poor hemodynamic profile yielded longer LOS for patients in ICU compared with CCU or ward. Besides, all kinds of inotropes were more frequently utilized in the ICU patients. Despite extensive utilization of many therapies, mortality was tripled among patients referred to ICU compared with ward patients, and of note, it was higher in ICU compared with CCU.

On the other hand, patients referred to CCU presented with a higher rate of pulmonary edema, more frequent history of coronary artery disease, more frequent presentation with acute coronary syndrome, more frequent use of beta-blockers and nitrates, and more frequent percutaneous intervention at index hospitalization compared with ICU or ward patients.

Therapeutic measures were evaluated in detail not only for the total population, as usually reported in most AHF surveys, but also for the first time in the different subgroups of patients including those in ICU. As expected, IV diuretics remained the most frequently utilized drugs for initial symptomatic treatment in all forms of AHF, followed by nitrates as vasodilators. Inotropes were also often administered in all participating countries to

26–51% of patients, despite a prevailing negative cardiologic opinion based on reports indicating possible adverse outcomes with frequently used drugs, such as dobutamine and milrinone [9, 10]. CPAP was used in 9.6% of studied patients and 16% required mechanical ventilation. The lower than expected prevalence of CPAP might be related to the fact that many centres in Europe do not utilize CPAP either because of lack of frequent practice and/or availability or to the severity of the patients that needed mechanical ventilation rather than CPAP. Of note, in the present survey, close to 50% of the ICU patients needed CPAP or mechanical ventilation.

Limitations of the ALARM-HF survey

Data collection in the participating hospitals was limited to 5–8 consecutive hospital discharges with a clinical diagnosis of AHF according to the ESC/ESICM classification of 2005. We note that there was a vast range in terms of organisation and quality of patient care. Therefore, we cannot assure that the cases included represent the overall AHF patient population in all countries. A diagnostic criterion was probably not always uniformly applied by all involved cardiologists and intensive care specialists. However, final adjudication to AHF subgroups was based on the completed data in the case reports which were compiled following discharge.

Indeed, our survey did not allow one to differentiate overlapping clinical characteristics, as in the case of pulmonary oedema between acute decompensated HF and hypertensive HF. Pulmonary oedema (PE) was actually a very frequent diagnosis, indicated by physicians in charge in 37% of our studied patients. Of note, PE was also an initial diagnosis in 49.6% in the Italian AHF survey [3]. Although the definition of PE is accepted worldwide, regional interpretations are indeed possible. We know that physicians could only quote one of the six items of the ESC classification. Very likely, patients with PE were derived from those with hypertensive HF and as well as those with pre-existing chronic systolic heart failure and our survey did not allow differentiation of either. This shows some of the limits of ESC/ESICM classification.

Another limitation is that the analysis of drug utilization and other therapeutic interventions relied on the case report forms without the possibility to compare the data with routine management guidelines in these hospitals. Therefore, our findings might be questioned with regards to representing established clinical practice. Long-term outcome data are also lacking. Because of the design of the ALARM-HF registry, which was based on anonymised data, a follow-up after hospital discharge was not possible.

Conclusion

Using pre-defined criteria, we compared initial findings, treatments and outcomes in a broad range of hospital settings in various regions of the world. Results of ALARM-HF designate that there are further distinct subgroups of patients beyond ESC/ESICM classification with graded severity of AHF. On the basis of the results derived from ALARM-HF, we conclude that the first episode of AHF is more deadly, and for the first time in the literature to the best of our knowledge, ICU patients differ from CCU and ward patients by having not only the poorest hemodynamics but also the worst prognosis. Those parameters should help in the future

stratification of patients for well-designed prospective randomized trials so that future progress in this difficult field occurs.

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